Moderate Lead Poisoning: Trends in Blood Lead Levels in Unchelated Children

Morri E. Markowitz,[1] Polly E. Bijur,[1] Holly A. Ruff,[1] Kenneth Balbi,[2] and John F. Rosen[1]

[1]Department of Pediatrics, Albert Einstein College of Medicine, Bronx, NY 10467 USA; [2]Montefiore Medical Center, Bronx, NY 10467 USA

The appropriate clinical management of children who are moderately poisoned with lead (Pb) is under active investigation. To determine the pattern of change in blood Pb (BPb) levels in the absence of chelation therapy, we followed moderately Pb-poisoned children (initial blood Pb level 1.21–2.66 µmol/l or 25–55 µg/dl) for 6 months with repeated BPb level measurements. Chelation therapy was not administered because all the children had negative lead mobilization tests indicating limited response to the chelating agent, calcium disodium edetate ($CaNa_2EDTA$). Eligible children received the following interventions: notification of the health department to remediate lead hazards; reinforced educational efforts about the toxicity sources and treatment of Pb during 10 clinic and 3 home visits; and iron therapy for children with ferritin levels less than 16 µg/l. To quantify the lead paint hazards in the home, we combined a visual rating of the surfaces (intact to peeling) with an X-ray fluorescence (XRF) measurement of the lead content of the painted surface. The sum of these assessments is termed the home environmental score (HES). Data were analyzed from 79 children. BPb levels declined by 27%, on average, over 6 months. HES was correlated with BPb at enrollment, but neither the initial nor later HES measurements predicted BPb at other time points. The HES was highest at enrollment and declined by 50% and 75% at the second and third home visits, respectively. However, only a minority of the children (20%) achieved an HES of 0, indicating no lead paint hazards at home. Despite some ongoing Pb exposure, a parallel fall in BPb levels was observed in subgroups of children with either initially low or high HES (above or below the median HES of 37). Iron status did not account for the change in BPb levels. These data provide evidence that our measure, the HES, is quantifiably related to BPb levels in children; that this correlation is significant only prior to intervention; and that BPb levels decline in children who are moderately poisoned with Pb after they are enrolled in a comprehensive intervention program, even in the absence of chelation therapy and in the presence of ongoing lead paint exposure and Fe deficiency. *Key words*: chelation, children, environment, exposure, iron, lead. *Environ Health Perspect* 104:968–972 (1996)

The appropriate clinical management of moderately Pb-poisoned children (BPb level 1.21–2.66 µmol/l or 25–55 µg/dl) is under active investigation. Several types of interventions have been correlated with at least transient declines in BPb. These include reduction of environmental Pb availability and chelation therapy. Several other aspects of treatment have theoretical advantages. Decreasing Pb ingestion through an alteration of behavior of both the child and the parents is a possibility that has been suggested but not formally tested. In addition, nutritional counseling to ensure dietary iron and calcium sufficiency should reduce the enhanced Pb absorption and retention associated with deficiency states in these minerals.

However, the relative weights of these factors in reducing BPb levels have not been defined. Even the efficacy of environmental and drug interventions in such children is not established. For example, 6 weeks after a course of chelation therapy was administered to moderately Pb-poisoned children, the decline in BPb levels was statistically indistinguishable from a nonchelated group with comparable initial BPb levels (*1*). Even studies correlating a fall in BPb levels to reduced environmental Pb exposure have not quantitated other possible explanations for the observation, e.g., changed behavior or improved metabolism (*2*).

In this report, we have focused on two factors that could explain change in BPb over time: exposure to leaded paint and Fe status. We selected and followed moderately Pb-poisoned children (initial blood Pb level 1.21–2.66 µmol/l or 25–55 µg/dl) for 6 months with repeated BPb level measurements. All the children underwent the lead mobilization test on at least one occasion; the results were negative, indicating limited response to the chelating agent, $CaNa_2EDTA$. Thus, none of these children qualified for or received chelation therapy.

We addressed the following questions: What is the magnitude of the correlation between home leaded paint exposure and BPb levels at the time moderately Pb-poisoned children are initially identified and arrive for medical management? In the absence of chelation therapy, is the subsequent trend in BPb levels predicted by ongoing exposure at home to leaded paint? Does Fe status or treatment of Fe deficiency affect the rate of BPb change?

Methods

Children referred to the Montefiore Medical Center Lead Clinic during the years 1986–1992 were potentially eligible for this study. The main aim of this research was to determine treatment outcomes in moderately Pb-poisoned children, defined at the time as those with blood lead (BPb) of 1.21–2.66 µmol/l (25–55 µg/dl) and an erthrocyte protoporphyrin (EP) ≥0.66 µmol/l (35 µg/dl). The main outcome measure was global intelligence, and those results have been reported elsewhere (*3*). Exclusion criteria included previous treatment and neurological or behavioral disorders from other causes. Informed consent was obtained from the parent or legal guardian.

All children received an 8-hour lead mobilization test (Pb-MT) at enrollment after undergoing a battery of tests that included psychometric assessment and electrophysiological measurements. The Pb-MT protocol has been reported elsewhere (*4*). Briefly, the Pb-MT consists of the administration of a single dose of calcium disodium edetate, 500 mg/m^2 given intramuscularly followed by an 8-hr urine collection for lead determination. All the children in this report excreted less than 200 µg/8 hr of Pb and had a ratio of urine Pb to drug dose less than 0.6, i.e., administration of the drug did not induce a lead diuresis.

The clinical program consisted of intensive medical and environmental follow-up. A total of 10 visits over 6 months was planned for each child. Initially, visits to the clinic were more frequent and occurred at enrollment and at 1 week, 4 weeks, 6 weeks, and 7 weeks later. Thereafter, visit frequency was reduced to every 4 weeks—at 12, 16, 20, and 24 weeks after enrollment. A final visit was scheduled for 25 weeks. The patient was seen at each visit by the pediatric nurse practitioners devoted to the project and by a housing specialist. Potential sources of lead were discussed with the parent as were routes of exposure, and information about nutrition and

Address correspondence to M. E. Markowitz, Department of Pediatrics, Montefiore Medical Center, 111 E. 210th Street, Bronx, New York 10467.

This work was completed at the affiliates of the Albert Einstein College of Medicine and supported by NIEHS grant ES04039 and W.T. Grant Foundation award 86109286.

Received 30 October 1995; accepted 8 May 1996.

hygiene was stressed. Blood was obtained for Pb determinations at each visit; ferritin was measured on blood samples from weeks 1, 7, and 24.

Three home visits were carried out by an X-ray fluorescence (XRF) specialist and a nurse practitioner: at enrollment, at 6 weeks, and at 24–25 weeks. At the home visit, each painted surface was assessed visually for its condition and scored on a 0–3 scale. A score of 0 was given to an intact surface; a score of 3 was given to a peeling surface. If the surface had bubbling or cracks, then a score of 1 or 2 was given, respectively. The lead content of the surface was measured in triplicate by XRF using an XK-3 instrument (Princeton Gamma Tech). Each surface of each room was tested at one location per surface; three replicate measurements were made at each site. No substrate correction was made since that was the standard at the time the study was initiated. Surfaces tested included all walls, windows, doors, and baseboards. Calibration procedures followed the manufacturer's recommendations and were performed hourly in triplicate using the standard block materials supplied by the manufacturer. The instrument was reset after each reading. Readings with this instrument are reported on a scale of 0–10 mg/cm^2. The mean of the three XK-3 readings for each surface was then multiplied by the visual rating. For example, an intact wall with an XK-3 reading of 10 had a score of 0 ($10 \times 0 = 0$). At the other extreme, a peeling surface with an XK-3 reading of 10 scored 30 ($10 \times 3 = 30$). The sum of all the products for an individual home was termed the home environmental score (HES). The number of surfaces assessed varied between homes. Because we did not quantify the amount of time a child spent in a particular room, the ratings were not weighted for a child's potential access to any surface, e.g., the child's bedroom did not have greater value than the living room.

After the homes were inspected, the following intervention was performed for all the subjects. The local Board of Health's Lead Bureau was notified. The Lead Bureau is responsible for the initiation and follow-up of the legal process needed to bring the home into compliance with existing health and housing codes. No specific abatement protocol was enforced. Educational efforts aimed at the parent or guardian about the sources of lead, its toxicity, and methods to reduce exposure were begun at the first clinic visit. In particular, efforts were made to remove the child from the lead source either by placement in alternative lead-free housing such as a relative's home, or by abatement of the primary residence. Nutritional counseling stressed the need for adequate calcium and Fe intake as well. Parents or guardians of children with ferritin levels <16 µg/l at enrollment were given sufficient Fe (Fer-in-sol) to provide the child with 5–6 mg/kg of elemental Fe daily for 3 months. No formal behavior modification program was used, and no quantitative assessment of any changes in parental or child behavior over the course of follow-up was made.

BPb was measured by graphite furnace atomic absorption spectrometry using a Varian Techtron atomic absorption spectrophotometer (*4*). The error of the method is ± 0.05 µmol/l (1 µg/dl); (95% confidence limits) for the blood range of these patients. Ferritin was measured by radioimmunoassay in sera obtained at 1, 7, and 24 weeks (*5*).

Data analyses included calculation of the means and standard deviations for the measures at each time point and determination of the differences across time. Log transformations of the HES scores were performed since the raw data were positively skewed. The transformed data were used for regression analyses.

Results

There were 206 children originally enrolled. Of these, 93 received at least one course of chelation. Of the remaining 113 children, 79 children, 1–7 years of age with initial BPb levels of 1.21–2.66 µmol/l (25–55 µg/dl) and negative Pb-MTs, completed the study. None had received chelation treatment prior to or during the study. The mean age at enrollment was 31.5 months. Approximately two-thirds of the children were of Hispanic origin and one-third were African American. They lived mainly in pre-1960 housing.

The HES scores are given in Table 1. The median score at the time of enrollment, 37, was used as a reference point to categorize the population into high- and low-level lead exposure. By the second home visit at 6–7 weeks, the mean and median scores had declined appreciably. There were no differences between the two groups on season of enrollment, age, or sex. Ten percent of the homes had an HES of 0 at enrollment, 25% at 6 weeks, and 20% at 6 months.

The mean BPb level was greater in the children with high HES scores at enrollment as compared to children with low HES scores (Fig. 1). BPb declined over time in a parallel manner in the two groups as reflected by a correlation between mean BPb levels over time of 0.98. When plotted as percent decline over time, the two curves were superimposed. In these children, the rate of decline was thus independent of initial HES levels.

A significant association between BPb and HES was noted at enrollment only (Table 2). Initial HES was not a predictor of BPb at 6 or 24 weeks or was HES related concurrently to BPb at the other two time points.

To assess whether age or initial ferritin explained the decline in BPb, multiple regression models were tested with age and ferritin as explanatory variables. Neither

Table 1. Home environmental scores (HES)

HES	Week 0	Week 6	Week 24
Minimum	0	0	0
Maximum	830	766	294
Mean ± SE	88 ± 16	44 ± 11	27 ± 5
Median	37	14	17

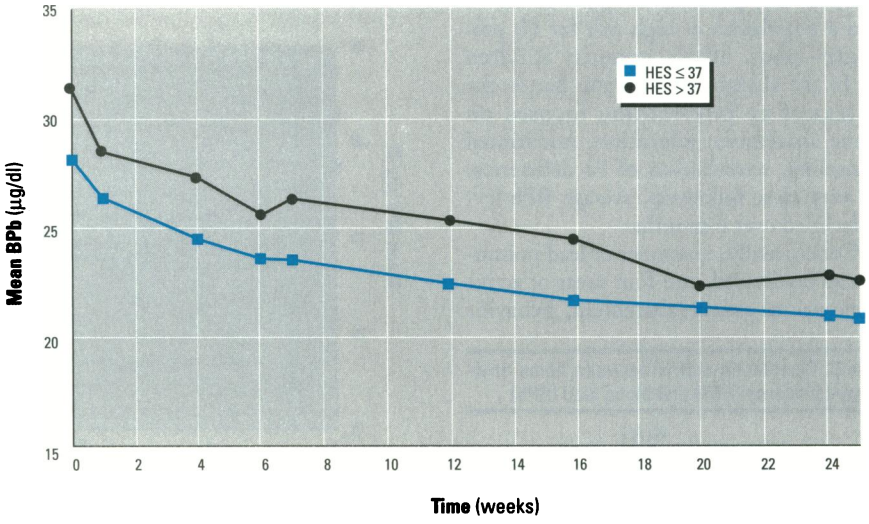

Figure 1. Average blood lead (BPb) levels over 6 months in children grouped above and below the initial median home environmental score (HES) of 37. $r = 0.98$.

age nor initial ferritin levels contributed significantly to the regression models. In addition, change in BPb from enrollment to completion at week 25 was unrelated to change in HES over the same time interval.

We further selected two subgroups of children who remained either persistently above or below the initial median HES of 37 throughout the study (12.5% of the entire sample in each group). As before, the children with high HES scores had higher initial BPb levels that declined over the six months, despite ongoing exposure, at a rate comparable to the low HES group (Fig. 2).

To test the hypothesis that change in Fe status as measured by ferritin levels could affect the rate of decline in BPb, we compared three subgroups: children who were Fe deficient throughout the 6 months, children with sufficient Fe throughout the 6 months, and children who were initially Fe deficient but were Fe sufficient by the end of the 6 months. BPb levels appeared to decline in parallel in the three groups (Fig. 3) with correlations of >0.9 between the mean BPb levels over time.

The frequency distribution for the two HES groups by BPb at the initial and final time points is given in Table 3. By 6 months, the BPb levels had declined to less than 1.21 µmol/l (25 µg/dl) in two-thirds of the children, regardless of HES group. This is the BPb cutoff for Pb-MT eligibility. Only 7% reached a BPb level less than 0.72 µmol/l (15 µg/dl); the lowest BPb achieved was 0.43 µmol/l (9 µg/dl) in one child.

Discussion

This study describes the trend in BPb levels in moderately Pb-poisoned children who were enrolled in a comprehensive Pb treatment program but were not eligible for chelation therapy. Our sample was drawn from a population at high risk for Pb poisoning—poor, urban, minority children (*6*). In the absence of chelation but in the context of an intervention focused on source abatement, education, nutritional counseling, remediation of Fe deficiency, and very close follow-up, average BPb levels declined over 6 months.

Conceptually, treatment of lead poisoning can be divided into four areas of active intervention: source abatement, behavior modification programs, metabolic manipulation by diet, and chelation. Of these, chelation and behavior modification were not offered to these children. In the absence of active interventions such as chelation or behavior modification therapy, others have reported that BPb levels may fall over time in moderately Pb-poisoned children. Over 6 months of observation, the reported decline has ranged from 7% to 18% (*7,8*). The decrease in BPb level in our group of 79 children in which there was intervention was somewhat larger at 27%. Initially BPb levels in this group were related to HES. In an extensive investigation of environmental Pb exposure in and around the homes of Cincinnati children, Clark et al. (*9*) found that an assessment of leaded paint hazards in the home correlated significantly with Pb washed from the children's hands and with children's BPb levels. The lead paint hazard was a measure that combined XRF wall measurements with an evaluation of the status of the surface. This measure appears comparable qualitatively to our HES. Similarly, we found a significant correlation of comparable magnitude between HES and BPb at the time of enrollment.

In our study, change in our environmental exposure measure, the HES, was not correlated to the change in BPb levels. In general, both BPb and HES declined over the 6 months. However, once children were enrolled in the study, average BPb levels declined even in the children with continuing, though decreased, lead exposure. At the extreme, the rate of fall in BPb levels of the subgroup of children with HES persistently greater than the initial median of 37 was the same as that of the children with minimal exposure through-

Table 2. Correlation matrix between home environmental scores (HES) and blood lead (BPb)

	R(*N*)		
BPb	HES week 0	HES week 6	HES week 24
Week 0	0.243 (77)*	—	—
Week 6	0.175 (78)	0.049 (75)	—
Week 24	0.111 (75)	0.048 (72)	0.136 (65)

*$P<0.05$.

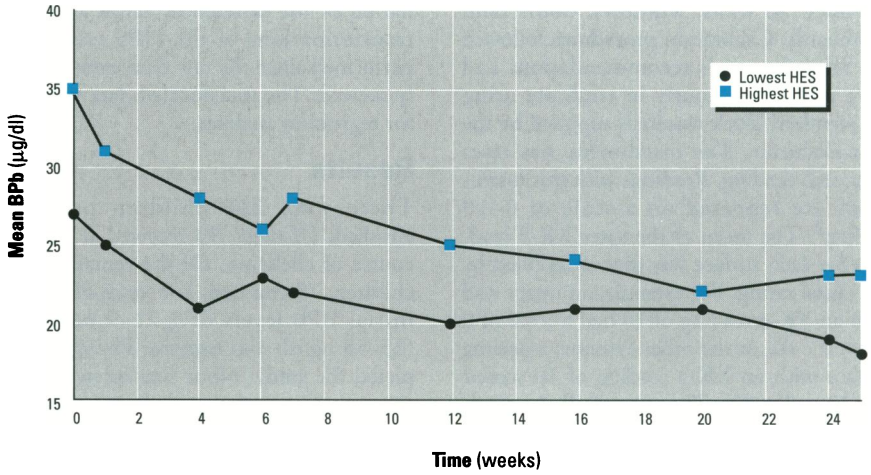

Figure 2. Average blood lead (BPb) levels over 6 months in two groups of children: those whose home environmental score (HES) was either persistently above or below the initial median value of 37 at all three home assessments. *R* between group at all time points = 0.89.

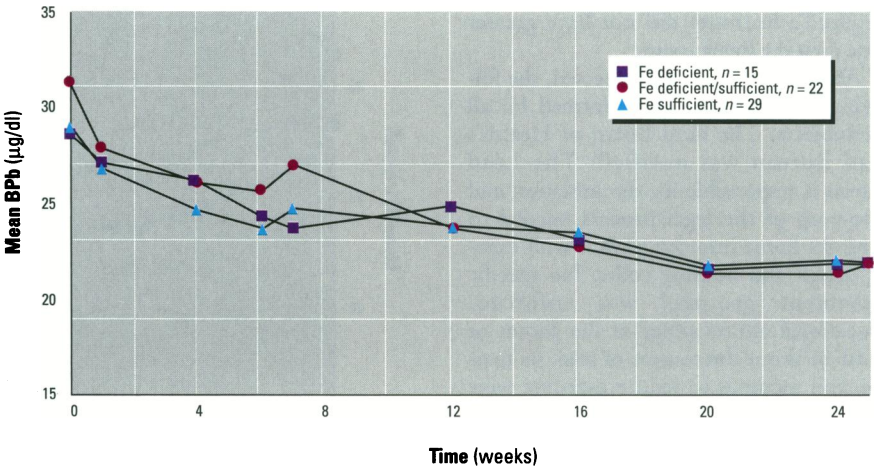

Figure 3. Average blood lead (BPb) levels over 6 months in children grouped by iron (ferritin) status as either iron deficient throughout the study period, iron sufficient throughout the study period, or initially iron deficient but iron sufficient by the end of the study period.

out the study period. Few of the homes of our children reached an HES of 0. Nevertheless, the continuing presence of some lead paint exposure in the children's homes did not preclude a decline in their BPb levels.

Other studies have examined the relationship between abatement and change in BPb levels but have not reported quantified measures of ongoing lead paint hazards (*2,10,11*). In these studies, abatement procedures differed and BPb levels either fell, remained the same, or transiently increased before falling (*2,10,11*). A more proximate measure of lead exposure, dust lead content, has been evaluated as a predictor of lead in blood and teeth (*2,12,13*). Testing different abatement protocols, Farfel and Chisolm (*12*) found little difference in dust Pb or BPb improvement over 6 months. Others have also failed to document a linear correlation between changes in leaded dust in the home environment and changes in BPb, although both declined over time (*2*). We did not measure the Pb content of the dust in the homes of our subjects; however, given the ongoing presence of lead paint hazards in the majority of homes even after 6 months, it is reasonable to postulate that Pb-contaminated dust remained in the home. Despite this likelihood, BPb levels declined. The implication of our observation is not that abatement procedures are unimportant, rather, that the presence of some environmental Pb does not preclude BPb concentration reductions. Arguably, our data support the notion that even incomplete remediation of lead hazards may benefit lead poisoned children.

Fe status did not account for the observed decline in BPb. The rate of change in BPb appeared comparable in the subgroups of Fe-deficient and -sufficient children and was not accelerated by correction of Fe deficiency. This is somewhat surprising because previous research has shown increased Pb absorption, retention, and toxicity in the presence of Fe deficiency (*5,14,15*). The effect of Fe status on BPb is relatively small and may be obscured by the magnitude of the lead burden, particularly in bone. Perhaps Fe status would show a greater effect in a less Pb-poisoned population.

Table 3. Frequency distribution (%) of home environmental scores (HES) and blood lead (BPb)

	HES ≤37		HES >37	
BPb (µg/dl)	Week 0	Week 25	Week 0	Week 25
<15	0	14	0	0
15–24	5	53	0	67
25–34	90	31	80	30
35–44	5	0	15	3
>44	0	3	5	0

To convert µg/dl to µmol/l, divide by 20.7.

Several other factors need to be considered. There is the seasonal variation in BPb levels reported by some (*2,7,8,16*) but not by others (*17*). In general, BPb levels are higher in the late summer and fall (*8*). Enrollment in our study occurred throughout the year and no effect of season could be discerned.

A second factor is age of the children. Pb levels tend to peak around 2 years of age (*6,16,18*). This age group has a greater prevalence of Fe deficiency and hand-to-mouth behavior, both predisposing factors, than older children. The average age at enrollment of our population was 31.5 months; thus, a decline based on the aging of our group was to be expected. However, the magnitude of the decline between 2 and 3 years of age reported in several longitudinal studies is considerably less (7%) than in ours (27%) (*16,18*).

Our study has limitations. No attempt was made to quantify the amount of time the child spent in the primary residence, and potential secondary sources of Pb exposure (e.g., at relatives' homes) were not determined. We also did not and could not assess the duration of exposure prior to enrollment. Though we documented one measure of exposure, the HES, we did not measure the Pb content of the dust in the rooms or on the hands of the child.

In the absence of chelation and in the presence of ongoing Pb exposure, average BPb levels still fell. Other aspects of our intervention may have contributed to this event, such as the educational and nutritional information provided at the frequent clinic visits. Each clinic visit included information about the sources and pathways of lead exposure and accumulation. Perhaps this resulted in improved household cleaning. Alternatively, the information provided to parents about the ingestion of leaded dust may have led them to wash the children's hands more often or to curb the children's hand-to-mouth behavior. As a speculation, different amounts of mouthing behavior may account, in part, for the observation that siblings with equal environmental lead exposure may have significantly different lead levels. These hypotheses remain to be tested. Staess et al. (*11*) made an indirect estimate of the effect of factors other than abatement and chelation that contribute to a change in BPb concentrations over 10–14 months. BPb levels declined 12% (35.1–30.9 µg/dl) in a group of unchelated children whose homes were not abated (*11*).

BPb in moderately Pb-poisoned children reflects the aggregate of environmental exposure (usually leaded paint or its dust), child behavior (pica, mouthing of toys and fingers), absorption (affected by iron and calcium status), distribution to and from other tissues (bone and soft tissues), and excretion (mainly in urine). In this study we focused on two of these components, environmental exposure and iron status, and found that neither component fully accounts for the observed decline in BPb levels in our unchelated children. The specific aspects of our comprehensive program that contribute to this decline have not been identified. What has been identified is a group of moderately Pb-poisoned children whose BPb levels decreased, even in the presence of lead in their homes, Fe deficiency, and no chelation. We suggest that future studies attempting to define factors most likely to affect BPb levels in children include 1) more proximal measures of environmental exposure such as hand dust Pb; 2) measures of body stores of lead in the child's skeleton, the major reservoir of lead in humans; and 3) quantitative measures of child behavior (such as hand-to-mouth activity and pica) and parental behavior (such as attention to the child's activities, diet, environment, and frequency of hand washing).

References

1. Markowitz ME, Bijur PE, Ruff H, Rosen JF. Effects of calcium disodium versenate ($CaNa_2EDTA$) chelation in moderate childhood lead poisoning. Pediatrics 92:265–271 (1993).
2. Charney E, Kessler B, Farfel M, Jackson D. Childhood lead poisoning: a controlled trial of the effect of dust-control measures on blood lead levels. N Engl J Med 309:1089–1093 (1983).
3. Ruff HA, Bijur PE, Markowitz ME, Ma YC, Rosen JF. Declining blood lead levels and cognitive changes in moderately lead-poisoned children. JAMA 269:1641–1646 (1993).
4. Markowitz ME, Rosen JF. Assessment of lead stores in children: validation of an 8-hour $CaNa_2EDTA$ provocative test. J Pediatr 104:337–341 (1984).
5. Markowitz ME, Rosen JF, Bijur PE. Effects of iron deficiency on lead excretion in children with moderate lead intoxication. J Pediatr 116:360–364 (1990).
6. Mahaffey KR, Annest JL, Roberts J, Murphy RS. National estimates of blood lead levels: United States, 1976–1980. Association with selected demographic and socioeconomic factors. N Engl J Med 307:573–579 (1982).
7. Klein MC, Schlageter M. Non-treatment of screened children with intermediate blood lead levels. Pediatrics 56:298-302 (1975).
8. McCusker J. Longitudinal changes in blood lead level in children and their relationship to season, age and exposure to paint or plaster. Am J Public Health 69:348–352 (1979).
9. Clark S, Bornschein R, Succop P, Roda S, Peace B. Urban lead exposures of children in

Cincinnati, Ohio. Chem Speciation Bioavailability 3(314):163–171 (1991).
10. Amitai Y, Brown MJ, Graef JW, Cosgrove E. Residential deleading: effects on the blood lead levels of lead-poisoned children. Pediatrics 88:893–897 (1991).
11. Staes C, Matte T, Copley CG, Flanders D, Binder S. Retrospective study of the impact of lead based paint hazard remediation on children's blood lead levels in St. Louis, Missouri. Am J Epidemiol 139:1016–1026 (1994).
12. Farfel MR, Chisolm JJ Jr. Health and environmental outcomes of traditional and modified practices for abatement of residential lead-based paint. Am J Public Health 80:1240–1245 (1990).
13. Alexander LM, Heaven A, Delves HT, Moreton J, Trenouth MJ. Relative exposure of children to lead from dust and drinking water. Arch Environ Health 48:392–400 (1993).
14. Watson WS, Hume R, Moore MR. Oral absorption of lead and iron. Lancet 2:236–237 (1980).
15. Barton JC, Conrad MEC, Harrison L. Effects of iron on the absorption and retention of lead. J Lab Clin Med 92:536–547 (1978).
16. McMichael AJ, Baghurst PA, Robertson EF, Vimpani GV, Wigg NR. The Port Pirie cohort study: blood lead concentrations in early childhood. Med J Aust 143:499–503 (1985).
17. Reigart JR, Whitlock NH. Longitudinal observation of the relationship between free erythrocyte porphyrins and whole blood lead. Pediatrics 57:54–59 (1976).
18. Dietrich KN, Berger OG, Succop PA. Lead exposure and the motor developmental status of urban six-year-old children in the Cincinnati prospective study. Pediatrics 91:301–307 (1993).